U.S. Department
of Transportation

**Research and
Special Programs
Administration**

400 Seventh Street, S.W.
Washington, D.C. 20590

JAN - 8 2001

Dr. James Harris
Research Consultant
TDM Labs, Inc.
2210 South Atlantic Avenue
Cocoa Beach, Florida 32931

Ref. No. 00-0359

Dear Dr. Harris:

This responds to your December 18, 2000 letter concerning requirements for shipping infectious substances under the Hazardous Materials Regulations (HMR; 49 CFR Parts 171-180). Specifically, you ask about requirements related to shipping blood plasma samples from HIV-infected patients for verifying the efficacy of drug therapies used to treat the HIV.

For purposes of the HMR, an "infectious substance" means a viable microorganism, or its toxin, that causes or may cause disease in humans or animals. The term includes agents listed in 42 CFR 72.3 of the regulations of the Department of Health and Human Services and any other agent that causes or may cause severe, disabling, or fatal disease. The samples you describe are not infectious substances under the HMR because the HIV has been completely inactivated by the addition of denatured alcohol to the samples.

To determine the hazard class of the samples you describe, you must test the sample mixture -- that is, the blood plasma plus denatured alcohol. It is not sufficient to class the sample based only on the characteristics of the denatured alcohol. If the blood plasma/denatured alcohol mixture does not meet the definition of a Class 3 (flammable liquid) material, or, indeed, any other hazard class, then the samples are not hazardous materials and, thus, not subject to any requirements under the HMR. See Subpart D of Part 173 of the HMR for definitions, classification criteria, and packing group assignments for hazardous materials other than explosives or radioactive materials.

If the blood plasma/denatured alcohol mixture meets the definition of a Class 3 material, you may ship small samples under the small quantity exception in § 173.4 of the HMR. Under this section, a small quantity of a Class 3 material is excepted from any other requirements of the HMR if it is packaged in accordance with the provisions of § 173.4. The packaging configuration you describe appears to conform to the requirements of this section. Note,

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however, that the completed package, as demonstrated by prototype testing, must be capable of successfully passing the performance tests in § 173.4(a)(6). In addition, the shipper must certify conformance with the requirements of § 173.4 by marking the outside of the package with the statement "This package conforms to 49 CFR 173.4."

I hope this information is helpful. If you have further questions, please do not hesitate to contact this office.

Sincerely,

Thomas G. Allan
Senior Transportation Regulations Specialist
Office of Hazardous Materials Standards

TDM Labs, Inc.

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"Excellence in Therapeutic Drug Monitoring"

Gorsky
§ 172.101 (D)
Diagnostic Specimens
00-0359

Sent by Courier

18 December 2000

Edward T. Mazzullo
Director
Office of Hazardous Material Standards
USDOT/RSPA (DHM 10)
400 Seventh Street, SW
Washington, DC 20590-0001

00 DEC 20 AM 8:51
DOT/RSPA/OHMS
EXEMPTIONS & APPROVALS

Dear Mr. Mazzullo,

This letter is meant to supplement the 14 December 2000 meeting between Susan Gorsky and Eileen Edmonson of your Office and Paul Lorch and I of our laboratory. In closing our meeting, it was agreed that a written response regarding our proposed business practices would be provided.

TDM Labs, Inc. will soon open as a CLIA-certified clinical reference laboratory. We specialize in the determination of the concentration of HIV medicines present in patient samples (it is common for HIV-infected patients to fail therapy because only subtherapeutic concentrations are achieved). Because the practice of modern HIV medicine requires rapid decisions, we must use overnight couriers (*e.g.*, FedEx, Airborne, *etc.*) to bring these samples to our facility. Our sample-submission protocol requires that the clinic staff mix completely 3 parts patient plasma with 7 parts denatured alcohol prior to packaging for shipment.

We had planned to offer the tests (to those physicians too distant from our facility to serve by land-based courier) with all the equipment necessary to ship the alcohol-containing patient sample to us as a infectious substance. As we added the costs, we concluded that the packaging, the shipper surcharges, and the real burden of completing accurately the shipper's declaration would collectively place the tests out of the reach of many patients. What is more, because the clinic staff must mix the patient plasma with denatured alcohol and because this chemical treatment is known to completely inactivate HIV (see below), we surmised that these shipments might be correctly labeled as something other than an infectious substance. Such was the genesis of our discussion at USDOT headquarters.

Please find enclosed three representative articles, each taken from the medical literature, that attest to the effectiveness of 70% alcohol (the remainder being either water or a water-based biological matrix such as plasma, serum, or blood) in completely inactivating the HIV virus. Attachment One is from The Journal of the American Medical Association, Volume 255, pages 1887-1891, and this document was published in 1986*.

* HTLV-III was the predecessor name for HIV.

Attachment Two is from Journal of Hospital Infection, Volume 28, pages 137-148, and this document was published in 1994. Attachment Three is from Journal of Hospital Infection, Volume 30, pages 167-180, and this document was published in 1995. These reports, written by three independent research groups from three continents and over a time span of approximately a decade, show that the alcohol treatment completely inactivates HIV. For your convenience, we have highlighted the discussion of the 70% alcohol treatment in each research report†. Based on a detailed assessment of the medical and scientific literature, the accuracy of these results has not been challenged.

To date, we have not shipped or received any samples. When we do, the shipping instructions will be as follows. Each treated sample will not exceed 4 milliliters in volume and the denatured alcohol that we use is, according to its manufacturer, a Packing Group II product. After mixing 3 parts of patient plasma with 7 parts of denatured alcohol, the physician (or physician's designee) is instructed to tightly seal the vial and to wrap adhesive tape around the closure. The vial is placed inside a liquid-tight bag along with sufficient adsorbent material to retain the entire contents in the event of a spill. These materials are then placed in a sturdy cardboard box along with appropriate cushioning materials. Depending on your response to this query, we may place the sturdy box inside a thick-walled, liquid-tight bag, designed for shipment of diagnostic specimens.

We look forward to receiving your letter that indicates to us how to legally categorize and label these proposed shipments. Please be specific as to whether USDOT would regard these as diagnostic specimens, as small quantity exceptions, or as some other category. We shall be pleased to answer any questions that you may have. I can be reached at the telephone number given above.

Sincerely,

James Harris, Ph.D.
Research Consultant

Enclosures
cc: Susan Gorsky
Eileen Edmonson

† A discussion of the use of denatured alcohol on HIV-contaminated surfaces is highlighted as well. Because alcohol evaporates rapidly when outside of a closed container (*e.g.*, when wiped as a thin film onto a surface), alcohol is less effective in the inactivation of HIV on surfaces. Hence, researchers differentiate between the performance of HIV inactivation in solution (in a closed container, evaporation does not occur) versus on surfaces (evaporation prevalent).